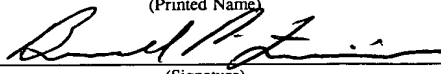


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Atty. Docket No. 072121-0139
TECH CENTER 1600-000
PATENT APPLICATION

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Paul A. RENHOWE, *et al.*
Title: HETEROCYCLIC COMPOUNDS
Appl. No.: 09/943,382
Filing Date: 08/30/2001
Examiner: R. Desai
Art Unit: 1625

CERTIFICATE OF FIRST CLASS MAIL I hereby certify that this correspondence is being sent via first class U.S. mail to Commissioner of Patents, Washington, D.C. 20231 on the date shown below. Bernard P. Friedrichsen (Printed Name)  (Signature) March 12, 2003 (Date of Deposit)
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**AMENDMENT AND RESPONSE TO
EX PARTE QUAYLE ACTION**

201B
Adharm
4/1/03

Commissioner of Patents
Washington, D.C. 20231

Dear Madam:

This is in reply to an Ex Parte Quayle Action mailed on December 18, 2002, imposing a restriction requirement in the above-captioned application. The shortened two month statutory period for response to the Office Action expired on February 18, 2002. With the attached Petition for one-month extension of time and the authorization to charge Deposit Account No. 50-2350 for the fee for a one-month extension of time, this response is timely filed.

Applicants thank Examiner Desai for her responsiveness in immediately transmitting a copy of the outstanding Ex Parte Quayle Action by facsimile to them on February 13, 2003, after Applicants advised her that they did not have a copy of the Office Action.

Applicants believe no fees in addition to the one-month extension of time fees are due for this filing. However, should any additional fees be due, the Patent Office is hereby authorized to charge any additional fees required for this filing or credit any

overpayment to Deposit Account No. 50-2350. For the purpose of charging or crediting said deposit account, duplicates of pages 1 and 2 and the signature page of this response are submitted herewith.

INTRODUCTORY REMARKS

Applicants first thank Examiner Desai for granting the telephonic interview of February 25, 2003, in which the scope of the claims and the expanded restriction requirement in the present Ex Parte Quayle Action were discussed.

A brief history of the prosecution of this application may be helpful. First, a restriction requirement was purportedly mailed to Applicants on April 17, 2002. Applicants did not receive the restriction requirement, but became aware of it on October 16, 2002 when using PAIR to check the status of the application. Upon request, Examiner Desai sent a copy of the April 17, 2002 restriction requirement to Applicant's attorney via facsimile. The restriction requirement divided the claims into six different groups, required that Applicants elect one Group for prosecution, and additionally required that Applicants elect a single disclosed species for prosecution. Groups I, II, and III each included claims 1-8 and 18, but divided independent claim 1 by defining what the variables in the chemical structure could be. Groups IV and V both included claims 9-17 and 20, but divided independent claim 9 by defining what the variables in the chemical structure could be. Finally, Group VI included claim 19 and 21 drawn to methods of treating diseases using the compounds of claims 1 and 9 of the other Groups. The specific restriction requirement imposed with respect to Groups I, II, and III is provided below:

I. Claims 1-8 and 18 all in part, drawn to compounds and pharmaceutical compositions of compounds of formula I wherein Y is $\text{NR}^{10}\text{R}^{11}$, OH, OR⁸, Z is NR^{13} , R¹ and R² do not together form a ring, all other R are non-hetero ring containing, classified in class 546, 514, subclass 272.8, 268.4, 322.

II. Claims 1-8 and 18 all in part, drawn to compounds and pharmaceutical compositions of compounds of formula I wherein Y is $\text{NR}^{10}\text{R}^{11}$, OH, OR⁸, Z is NR^{13} , R¹ and R², together form a ring, containing S or O as a hetero atom all other R are non-hetero ring, classified in class 546, 514, subclass 114, 115, 300.

III. Claims 1-8 and 18 all in part, drawn to compounds and pharmaceutical compositions of compounds of formula I other than in Groups I and II, classified in various classes and subclasses.

On October 17, 2002, Applicants filed a Response to Restriction Requirement along with a 5-month petition for extension of time shortly after they became aware of the outstanding restriction requirement. In the Response, Applicants elected the claims of Group III, elected a species as required, and canceled claims 9-17, 20, and 21. Applicants also noted that Group I was an improper group because it required that R¹ and R² do not together form a ring when claim 1 specifically sets forth that they do form a ring. Applicants also noted that claim 19 should be rejoined with Group III because it is directed to method of treating that uses the compound of claim 1.

An Ex Parte Quayle Action, responsive to Applicant's October 17, 2002 Response, was purportedly mailed to Applicants on December 18, 2002. Examiner Desai sent a copy of the Action to Applicant's attorney via facsimile on February 13, 2003, when Applicants became aware of the Action while using PAIR. In the Ex Parte Quayle Action, the Examiner (1) required that the title of the application be changed, (2) imposed additional restriction requirements to the only independent claim of elected Group III, (3) rejoined claim 19 with the compound claims, (4) objected to claims 2-4 for failing to further limit the further restricted claim 1, (5) noted that claims 1, 5-8 and 18 and 19 would be allowable if amended to exclude the non-elected subject matter, (6) analyzed the closest prior art found by the Examiner, and (7) closed prosecution on the merits. Applicants respectfully contend that this is an improper Ex Parte Quayle Action. As noted in § 714.14 of the MPEP, an Ex Parte Quayle Action should be issued only when all claims in an application have been allowed and only formal matters remain. Here, the Examiner has imposed an additional particularly onerous restriction requirement without providing Applicants with any ability to respond or for that matter even decide what Group they would elect. In other words, the Examiner has decided to rewrite the single independent claim. Applicants have paid the requisite filing fees and are entitled to examination of the application and the remaining claims after the initial restriction requirement. It is grossly unfair and improper (see § 803.02 of the MPEP) that, in an Ex Parte Quayle Action, the

various Markush groups of the single independent claim should be narrowed so severely that none of the other dependent compound claims (claims 2-8) even fall within the scope of the narrowed claim. This is particularly true given that there has been no prior art cited which is relevant to the patentability of the elected species or even claim 1 as it was filed. What the Examiner has done is analogous to rejecting each of the claims in a final rejection before Examination has even begun even though the closest prior art cited by the Examiner is not relevant to the pending claims.

Because Applicants are reasonable, were uncertain about the specific extent of the newly-imposed restriction on the compounds of Group I, and felt that such restrictions were particularly burdensome and yet might be resolved by telephonic interview, Applicants requested a telephonic interview with the Examiner. During the interview, Examiner Desai and Applicant's attorneys came to a general understanding regarding some aspects of the expanded restriction requirement. However, Applicants respectfully assert that they are entitled to broader claim coverage and scope than that imposed by the expanded restriction requirement. Therefore, Applicants respectfully traverse the expanded restriction requirement imposed in the Ex Parte Quayle Action. Because complete agreement was not reached, Examiner Desai suggested that Applicants file the present Amendment and Response to Ex Parte Quayle Action. Applicants hereby reserve the right to challenge the Ex Parte Quayle Action.

STATUS OF CLAIMS AND AMENDMENT

Claims 1-8, 18, and 19 are currently pending in this application. Claims 9-17, 20, and 21 were canceled in Applicant's Response to Restriction Requirement filed on October 17, 2002. The Examiner rejoined claim 19 with compound claims 1-8 and 18 in the Ex Parte Quayle Action. The title is amended as required by the Examiner in the Ex Parte Quayle Action. Claim 1 is amended in part based on the Examiner's newly expanded restriction requirement. Claims 2, 3, 4, and 5 are amended based on the amendment of claim 1. New claims 22-29 are added by this Response. Each of new claims 22-29 depend from independent claim 1 or from dependent claim 4 which depends from claim 1 and include each and every feature of independent claim 1. Therefore, no new search should be

required. Support for amended claims 2, 3, 4, and 5 and new claims 22-29 is found through the specification and claims as filed, including, but not limited to the following:

- claim 2: paragraph 78;
- claim 3: paragraph 78;
- claim 4: paragraphs 80, 82, and 101;
- claim 5: claim 5 as originally filed and paragraph 84;
- claim 22: paragraph 78;
- claim 23: paragraph 78;
- claim 24: paragraph 81;
- claim 25: paragraph 81;
- claim 26: paragraph 85;
- claim 27: paragraph 85;
- claim 28: paragraph 85; and
- claim 29: paragraph 79.

In view of the following remarks and amendments, Applicants respectfully submit that the application is in condition for allowance.

REMARKS REGARDING RESTRICTION REQUIREMENT AND PRIOR ART CITED BY EXAMINER

During the interview of February 25, 2003, Examiner Desai clarified the expanded restriction requirement which was imposed on the claims of the application. Examiner Desai explained that the following new restrictions were imposed on the compounds of the single independent claim (claim 1) of Group III:

1. Y is a $\text{NR}^{10}\text{R}^{11}$ group;
2. Z is a NR^{13} group;
3. R^1 and R^2 join together to form a substituted or unsubstituted 6-membered ring comprising at least one O, N, or S atom;
4. One of R^5 and R^6 is a heterocyclic ring and the other of R^5 and R^6 is H; and

5. All other R groups are non-heterocyclic groups and non-heterocyclic ring containing groups.

Applicants respectfully assert that they are entitled to broader claim coverage than that imposed by the expanded restriction requirement. Therefore, Applicants respectfully traverse the restriction requirement. However, in order to obtain rapid allowance, Applicants have amended claim 1 in accordance with paragraphs 1-3 as set forth above. Applicants respectfully request reconsideration of the newly imposed restriction requirement and request that the restriction with respect to paragraphs 4 and 5 be withdrawn for the reasons presented below.

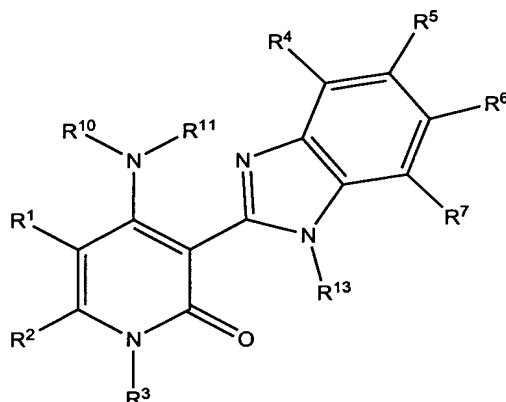
In the Ex Parte Quayle Action, the Examiner objects to claims 2-4 alleging that they fail to further limit the subject matter of a previous claim. The Action states that amended claim 1 will render claims 2-4 duplicates of claim 1. The Office Action thus requires cancellation of claims 2-4. The Office Action next objects to compound claims 1, and 5-8 as containing non-elected subject matter, but it also notes that compound claims 1, and 5-8 are allowable over the prior art of record. Applicants respectfully note that if claim 1 is amended in strict compliance with the newly-imposed restriction requirement suggested by the Examiner in paragraphs 1-5, then none of claims 2-8 will be of proper dependent form due to the highly restrictive and overly extensive narrowing of the independent claim. This demonstrates the unreasonable nature of the newly imposed restriction requirement and explains why the new restriction requirement is so highly burdensome to Applicants. Although Applicants are reasonable and are willing to amend claim 1 in compliance with paragraphs 1-3 to obtain rapid allowance, Applicants simply cannot amend claim 1 as specified in paragraphs 4 and 5.

According to the Ex Parte Quayle Action, the closest prior art with respect to claim 1 is WO 01/28993 and U.S. Patent No. 6,479,512. The Examiner includes the chemical structures of these compounds in the Ex Parte Quayle Action and specifically notes with respect to the Y group of claim 1 of the present application, that "the substitution on the 4th position of the N of the quinoline group is H rather than the NR¹⁰R¹¹ group of the instant invention". In other words, the Examiner is stating that Y is an H in the cited prior art. Notably, however, H is not included in the Markush group that defines

Y in claim 1 as it was filed. Also noted in the Ex Parte Quayle Action is WO 01/29025. As noted by the Examiner, the structure provided with respect to this reference "has an indole instead of a benzimidazole". Applicants further note that the substitution at the 4th position of the quinolinone in the structure provided by the Examiner with respect to WO 01/29025 is H rather than an NR¹⁰R¹¹ group. In other words, in each of the structures cited by the Examiner, Y is an H. For this reason, Applicants respectfully contend that they should be entitled to significantly broader claim coverage than that imposed in the new expanded restriction requirement. In other words, the prior art cited by the Examiner indicates that Applicants are entitled to broader coverage rather than the extremely narrow coverage imposed in the new restriction requirement.

Although it is Applicant's position that claim 1 should not have to be amended at all, in the interest of obtaining rapid allowance, Applicants are willing to amend independent claim 1 to comply with paragraphs 1-3 such that Y is an NR¹⁰R¹¹ group, Z is an NR¹³ group, and such that R¹ and R² join together to form a substituted or unsubstituted 6-membered ring comprising at least one O, N, or S atom. Applicants particularly assert that the amendment regarding R¹ and R² is unnecessary and improper. Although Applicants are willing to comply with the new requirements set forth in paragraphs 1-3, they simply cannot amend the claims to require that one of R⁵ and R⁶ is a heterocyclic ring and the other of R⁵ and R⁶ is H; and to require that all other R groups are non-heterocyclic groups and non-heterocyclic ring containing groups as these requirement are too burdensome and restrictive to abide. Applicants simply should not and cannot be forced to amend independent claim 1 to be so narrow that each of the dependent compound claims must be canceled. This is especially true when, as here, there is no cited prior art with a chemical structure that is even close to that set forth by claim 1 prior to amendment.

Applicants respectfully contend that their amendment of claim 1 provides an adequate chemical scaffold that can be readily searched and which should be sufficient to allow the Examiner to perform a rapid and simple search for the compound. This scaffold is shown below:



where R¹ and R² join to form a 6-membered substituted or unsubstituted ring comprising at least one O, N, or S atom.

Although Applicants respectfully contend that claim 1 could be searched and examined prior to the current amendment, Applicants note that a structure search that includes the above scaffold with the R¹ and R² limitation that they join to form a 6-membered substituted or unsubstituted ring comprising at least one O, N, or S atom should allow the Examiner to examine the claims without imposing a serious burden upon her. For this reason, any further restriction of the independent claim is not proper under § 803 of the MPEP which states that two criteria must be met for any restriction requirement to be proper. First, the inventions must be independent or distinct as claimed. Second, there must be a serious burden on the Examiner. As noted in § 803 of the MPEP, "If the search and examination of an entire application can be made without serious burden, the Examiner must examine it on the merits..."

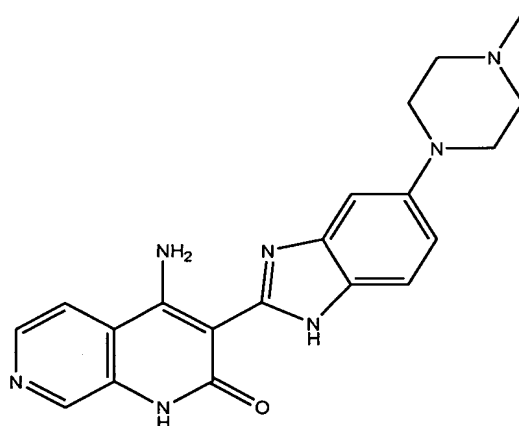
Applicants respectfully direct the Examiner's attention to § 803.02 of the MPEP which describes restriction practice when Markush groups are present. As stated in this section of the MPEP,

Since the decisions in *In re Weber*, 580 F.2d 455, 198 USPQ 328 (CCPA 1978) and *In re Haas*, 580 F.2d 461, 198 USPQ 334 (CCPA 1978), it is improper for the Office to refuse to examine that which applicants regard as their invention, unless the subject matter in a claim lacks unity of invention. *In re Harnish*, 631 F.2d 716, 206 USPQ 300 (CCPA 1980) and *Ex parte Hozumi*, 3 USPQ2d 1059 (Bd. Pat. App. & Int. 1984). Broadly, unity of invention exists where compounds included within a Markush group (1) share a common utility, and (2)

share a substantial structural feature disclosed as being essential to that utility.

(underlining added for emphasis)

According to the MPEP and the cases cited above, Applicants respectfully contend that the imposed restriction requirement is improper. As noted in § 803.02, a Markush type claim may even include independent and distinct inventions. As explained in § 803.02 of the MPEP, an examiner may require a provisional election of a single disclosed species prior to examination on the merits as was done in the previous Restriction Requirement. As required, Applicants elected the species 4-amino-3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]-1,7-naphthyridin-2(1H)-one in their Response dated October 17, 2003, the structure of which is shown below:



As further explained in § 803.02 of the MPEP,

Following election, the Markush-type claim will be examined fully with respect to the elected species and further to the extent necessary to determine patentability. If the Markush-type claim is not allowable over the prior art, examination will be limited to the Markush-type claim and claims to the elected species, with claims drawn to species patentably distinct from the elected species held withdrawn from further consideration.

(underlining added for emphasis)

In the case at hand, however, and explained above, none of the structures in the prior art cited by the Examiner is relevant to the patentability of the elected species or indeed claim 1 as it was filed. In other words, the Examiner has found no prior art that anticipates or renders obvious the elected species. Therefore, rather than impose a new restriction

requirement on claim 1, the following excerpt from § 803.02 of the MPEP applies,

On the other hand, should no prior art be found that anticipates or renders obvious the elected species, the search of the Markush-type claim will be extended. If prior art is then found that anticipates or renders obvious the Markush-type claim with respect to a *non-elected species*, the Markush-type claim shall be rejected and claims to the nonelected species held withdrawn from further consideration. The prior art search, however, will not be extended unnecessarily to cover all nonelected species. Should applicant, in response to this rejection of the Markush-type claim overcome the rejection, as by amending the Markush-type claim to exclude the species anticipated or rendered obvious by the prior art, the amended Markush-type claim will be reexamined. The prior art search will be extended to the extent necessary to determine patentability of the Markush-type claim. In the event prior art is found during the reexamination that anticipates or renders obvious the amended Markush-type claim, the claim will be rejected and the action made final.

(underlining added for emphasis)

Obviously, should no prior art be found during the extended search required under § 803.02 of the MPEP and already performed by the Examiner, then the claims should be allowed.

For the reasons presented above, Applicants respectfully request that the Examiner reconsider the full extent of the newly-imposed restriction requirement and allow the claims as amended if no relevant prior art can be found.

EXPLANATION OF AMENDMENTS

I. Amendment of Title

The title has been amended to read “Heterocyclic Derivatives of Quinolinone Benzimidazoles”. Applicants respectfully request that the Examiner accept the newly amended title.

II. Explanation of Amendment of Claim 1

Claim 1 has been amended as follows based on the expanded restriction requirement imposed by the Examiner:

1. In accordance with the Examiner's newly-imposed restriction requirement and clarification during the February 25, 2003 telephone interview, the Markush group defining Y has been significantly amended so that Y is currently defined as an $-NR^{10}R^{11}$ group.
2. In accordance with the Examiner's newly-imposed restriction requirement and clarification during the February 25, 2003 telephone interview, the Markush group defining Z has been significantly amended so that Z is currently defined as an NR^{13} group.
3. The paragraph relating to R^1 and R^2 has been amended in accordance with the Examiner's newly-imposed restriction requirement to read that R^1 and R^2 join to form a 6 membered substituted or unsubstituted ring comprising at least one O, N, or S atom.
4. The spelling of "heterocylyoxy" in the paragraph relating to R^3 and R^{13} has been corrected to read "heterocyclyoxy".
5. The paragraph relating to R^8 has been deleted. This was required because $-OR^8$ was deleted from the choices for Y in the Markush group related to Y choices.
6. The paragraph relating to R^9 and R^{18} has been deleted from its original location in the claim. This was necessary because $-SR^9$ was deleted from the choices for Y in the Markush group related to Y choices. R^9 was removed from the paragraph and the resulting new paragraph was inserted at the end of the claim where it now fits with respect to R^{18} .
7. The paragraph relating to R^{12} has been deleted. This was required because $-C(=O)-R^{12}$ was deleted from the choices for Y in the Markush group related to Y choices.

8. The word "and" was removed from the paragraph related to R¹⁶ and inserted into the paragraph related to R¹⁷, R¹⁹, and R²⁰ to make the claim read grammatically correct with the insertion of the R¹⁸ paragraph described in (6) above.

9. Applicants have not amended claim 1 to require that one of R⁵ or R⁶ is a heterocyclic ring and that the other of R⁵ or R⁶ is a H. Applicants have also not amended claim 1 to require that all other R groups not include heterocyclic groups. As noted above, Applicants respectfully submit that this further narrowing of the only independent claim is unjustified, overly burdensome to Applicants, and simply not needed. Applicants respectfully note that if these additional amendments are imposed upon claim 1, then none of the dependent claims prior to the present amendment (claims 2-8) is a proper dependent claim.

III. Explanation of Amendment of Claims 2-4

Claims 2-4 were objected to in the Ex Parte Quayle Action as failing to further define the subject matter of claim 1. Claims 2-4 are amended to make them proper dependent claims based upon the amendment of claim 1.

IV. Explanation of Amendment of Claims 5-8

Claim 5 is amended to make it a proper dependent claim based upon the Examiner's newly-imposed restriction requirement. In addition, each of claims 5-8 are amended to depend from dependent claim 4 rather than independent claim 1.

V. Addition of New Claims 22-29

Applicants have reviewed the specification and have added new claims 22-29 for which there is adequate support. These claims each depend from amended independent claim 1 through dependent claim 4 and further define the scope of the claim in a proper manner. Therefore, no new search should be required for these claims. Applicants respectfully request that the new claim be entered into the application.

AMENDMENTS

Please amend the title to read as follows:

--Heterocyclic Derivatives of Quinolinone Benzimidazoles--